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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/724,135	11/28/2000	Eileen Louise Rice McFarland	2727.1001-000	6130

21005 7590 03/26/2002

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EXAMINER
PADMANABHAN, KARTIC

ART UNIT	PAPER NUMBER
1641	10

DATE MAILED: 03/26/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/724,135	MCFARLAND, EILEEN LOUISE RICE	
	Examiner	Art Unit	
	Kartic Padmanabhan	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 February 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 1-13 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Applicant's invention is drawn to a method of determining predisposition to psychosis by measuring the presence of anti-cw antibodies in a sample. However, many dispositions, outside the realm of psychotic disorders may be determined by measuring these antibodies. For example, numerous studies, including Curtin et al., (Am. J. Medical Tech., 1967) Mouro et al. (Blood, 1995), and Bowman et al. (Vox Sang, 1993) disclose the measurement of these antibodies for the determination of hemolytic disease. Therefore, how can the determination of the same antibodies be used to determine psychosis with the exclusion of other disorders related to cw antibody presence? The current state of the art does not enable the undertaking of a method or kit for this purpose. Further, since Cw is relatively rare and no previous definitive correlation has been demonstrated between the measurement of cw antibodies and psychosis, a method attempting to link the two inherently encompasses a great amount of uncertainty, which the current state of the art is unable to remedy. In addition, there is insufficient guidance and working examples in the specification to enable one of skill in the art to determine predisposition to psychosis by measuring anti-cw antibodies. The one case study

with only 1 subject referenced in the specification is grossly insufficient to meet this criterion of enablement. The results from one case study cannot possibly be used as a definitive statement that the method of applicant can be used in all cases and populations to determine predisposition to psychosis. Results of case studies must be readily reproducible, which has not been established in this instance. Especially when considering that only one patient was followed in the case study, the onset of schizophrenia could have occurred by chance and not due to the presence of anti-cw antibodies. In addition, the disclosure of applicant has not enabled the determination of predisposition to all types of psychosis. Since the many psychotic disorders affect the body through different mechanisms that may differ greatly, it is unclear how one could use one method to determine predisposition to all these disorders. Applicant has certainly not elucidated that issue in the specification. Further, applicant has only provided one example with a patient who developed schizophrenia, which is insufficient to enable all types of psychosis. Therefore, undue experimentation would be required of one of skill in the art to practice the invention commensurate with the full scope of the claims.

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1-5 and 11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

5. Claim 1 recites the limitations "the diagnosis" and “the progeny’s mother”. There is insufficient antecedent basis for these limitations in the claim.

6. Claim 5 recites the limitation "the same". There is insufficient antecedent basis for this limitation in the claim.

7. Claim 11 recites the limitation "the diagnosis". There is insufficient antecedent basis for this limitation in the claim.

Response to Arguments

8. Applicant's arguments filed 2/27/02 have been fully considered but they are not persuasive.

9. First of all, applicant acknowledges that the claimed method "***can be*** indicative of a predisposition to psychosis" (page 3 of the response), which inherently indicates that the claimed method may not work. For the invention to be enabled, the claimed method must work. In addition, applicant argues that the Mouro, Curtin, and Bowman references, which are used as support in asserting that the claimed invention is not enabled, do not teach applicant's invention. The examiner acknowledges this fact, as these references were not applied under 35 USC 102 and/or 35 USC 103. Although the examiner agrees that the hemolytic diseases discussed in these references may be indicative of the adverse effects of histocompatability, the examiner maintains that one cannot differentiate between psychosis and hemolytic disease based on the claimed method of applicant, which was the only reason that these references were cited.

10. Applicant also alluded to several publications in support of their contention that the state of the art does indeed enable their claimed method. This argument is unconvincing. Firstly, with respect to the argument that the Wright reference establishes a link between HLA and psychosis, the examiner notes that the Wright reference states, "a susceptibility locus ***may exist*** and it may be within the HLA region, but again the evidence is ***far from conclusive***". This

disclosure in the reference clearly indicates that no such link has been definitively established, but rather, merely postulated. With regards to the Lindholm study, applicant argues that the reference reports the presence of a schizophrenia-susceptibility locus. However, this study only focused on 1 pedigree, and other genetic factors native to that pedigree may have influenced onset of psychosis. The authors of this study also recognize the need for further study before drawing any definite conclusions about the relationship between the gene and schizophrenia.

11. Applicant also argues that the Bassett and Lahdelma references help support their claims of the enablement of the present claims because the references discloses associations between HLA and schizophrenia. Thereby rendering the one case in applicant's specification sufficient to enable the claimed invention. The Bassett study states that a minority of patients with schizophrenia may have 22qDS, but they acknowledge that no casual genes have been identified and this is only one subtype of schizophrenia. Further, it is noted that the studies alluded to by Basset et al. in support of their contention only found 1 case and 2 ~~eaes~~ cases of schizophrenia with 22qDS. Both these studies employed sample sizes of less than 30, which precludes the obtainment of statistically significant results. One or two cases can easily be attributed to background prevalence of the gene. Basset et al. also acknowledge that many investigations are still necessary to determine the relationship of a 22qDS subtype to schizophrenia. With respect to the Lahdelma reference, that study only employed subjects who already had schizophrenia. Therefore, no meaningful conclusions can be drawn ab0ut predisposition to a disorder if the patients already have the disorder. The proper temporal relationship has not been established. In addition, this study has little, if any relevance, to applicant's claims as the reference is only determining differences in treatment response between different groups of patients who already

have a disorder. The reference still recognizes that studies have been unable to confirm the connection between HLA and schizophrenia. Even Lahdelma et al. "could not find any altered frequency of HLA-A1 among schizophrenic patients in general". In addition, this study was only done on the Finnish population, and the authors recognize that the same association found in the study may not be found in other populations, which makes it impossible to extrapolate their results to create a general method of assessing predisposition to a psychotic disorder.

12. With respect to the Chowdari reference, it is noted that the authors indicate that their results suggest a susceptibility locus for schizophrenia in the HLA region, but their results are limited to the Chinese, and they acknowledge that further clarification is necessary. They also state that "an autoimmune pathology for schizophrenia is plausible, though persuasive evidence is unavailable", and genome linkage studies "have not yielded consistent results for schizophrenia". They also state that "the question of HLA association with schizophrenia is unresolved".

Therefore, for the all the reasons discussed above, applicant's arguments that the state of the art allows for the practice of their invention without undue experimentation, thereby rendering the claimed invention unable, is unconvincing. In fact, an association between anti-cw antibodies and predisposition to psychosis has not been established with any consistency. Further, it is noted that the present claims are not restricted to specific populations, or even to schizophrenia, to which applicant's discussion was limited. The examiner maintains the position that although undue experimentation would not be required to measure anti-cw antibodies, it would be required to establish a definitive or any casual link between those antibodies and a predisposition to psychosis. Even in the one example provided by applicants, a number of years

were required before a diagnosis of schizophrenia was made. In addition, the state of the art does not enable the diagnosis of a predisposition to psychosis. As applicant acknowledges, the prior art does not establish a link between anti-cw antibodies and psychosis. If it had, the reference would qualify under the appropriate section of 35 USC 102. Applicant's reliance on the case study present in the specification is insufficient to provide adequate predictability, guidance, and working examples. As discussed previously, applicant has shown the results of one individual possessing anti-cw antibodies who later developed schizophrenia. This result may have occurred by chance. Since a study of many individuals from multiple studies has not been provided, applicant has not enabled the determination of a predisposition to psychosis. Further, applicant's arguments that the effect of the anti-cw antibody and not the mere presence of the antibody is the determining factor is also unconvincing to provide ennoblement for the recited claims. The presence of the antibody renders the fact that it will exert some effect inherent.

Conclusion

Claims 1-13 are rejected.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period

will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kartic Padmanabhan whose telephone number is 703-305-0509. The examiner can normally be reached on M-F (8:30-5:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 703-305-3399. The fax phone numbers for the organization where this application or proceeding is assigned are 703-746-5207 for regular communications and 703-305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Kartic Padmanabhan
Patent Examiner
Art Unit 1641

*** KP

March 13, 2002

BAO-THUY L. NGUYEN
PRIMARY EXAMINER
3/21/02